REMARKS

After the entry of the foregoing amendments, claims 1-9 and 28 will remain pending. Claims 4-7 and 10-27 are canceled herein, without prejudice. New claim 28 is directed to the use of a fluorescent unsymmetrical cyanine dye. Support for claim 28 may be found in the specification at page 17 lines 9-19. Claim 1 is amended to more clearly define the invention. Claim 1 has been amended to clarify that the method for detecting molecules expressing a selected epitope in a sample comprises:

(a) immobilizing a molecule expressing a selected epitope in a sample to a solid support;

(b) contacting the solid support with a molecule that specifically binds to the selected epitope, streptavidin and a biotinylated oligonucleotide, wherein the molecule that specifically binds to the selected epitope is ~~a biotinylated monoclonal antibody, a biotinylated FAb, a biotinylated F(Ab)2, a biotinylated humanized or chimeric antibody with or without a human Fc, a biotinylated single chain Fv, a biotinylated constrained epitope specific CDR, a biotinylated CDR mimetic, a biotinylated engineered CDR structure,~~ a monoclonal antibody that comprises a universal epitope, a FAb that comprises a universal epitope, a $F(Ab)_2$ that comprises a universal epitope, humanized or chimeric antibody that comprises a universal epitope, a single chain Fv that comprises a universal epitope, a constrained epitope specific CDR that comprises a universal epitope, a CDR mimetic that comprises a universal epitope, or a engineered CDR structure that comprises a universal epitope, wherein ~~if the molecule that specifically binds to the selected epitope is a monoclonal antibody that comprises a universal epitope, a FAb that comprises a universal epitope, a F(Ab)2 that comprises a universal epitope, humanized or chimeric antibody that comprises a universal epitope, a single chain Fv that comprises a universal epitope, a constrained epitope specific CDR that comprises a universal epitope, a CDR mimetic that comprises a universal epitope, or a biotinylated engineered CDR structure that comprises a universal epitope,~~ the solid support is additionally contacted with a biotinylated molecule that binds to the universal epitope, wherein the biotinylated molecule that binds to the universal epitope is a biotinylated monoclonal antibody, a biotinylated FAb, a biotinylated $F(Ab)_2$, a biotinylated humanized or chimeric antibody preferably with or without a human Fc a biotinylated single chain Fv, a

biotinylated constrained epitope specific CDR, a biotinylated CDR mimetic, or a biotinylated engineered CDR structure,

whereby the molecule that specifically binds to the selected epitope binds to the selected epitope of the molecule immobilized to the solid support and~~, if it is biotinylated, to the streptavidin which binds to the biotinylated oligonucleotide that comprises an RNA polymerase promoter, and if it comprises a universal epitope,~~ to the biotinylated molecule that binds to the universal epitope which binds to the streptavidin which binds to the biotinylated oligonucleotide that comprises an RNA polymerase promoter ;

(c) amplifying the oligonucleotide by RNA amplification to produce an RNA amplification product that is not labeled with a radioactive label or a fluorescent label;

(d) contacting ~~the~~ said amplified oligonucleotide with a fluorescent dye which stains the RNA amplification product; and

(e) detecting fluorescence emitted from the stained RNA amplification product that ~~is indicative~~ allows linear quantification of the molecule comprising the selected epitope being present in the sample.

Support for these amendments is found in the specification in Example 1, page 26.

No new matter is added.

Obviousness-Type Double Patenting

Claims 1-9 are rejected on the grounds of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-11 of U.S. 7,524,628; over claims 1-16 of U.S. 7,045,286 in view of U.S. 5,922,553; over claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. 7,361,464; and over claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. 7,341,831. Claims 4-7 have been canceled. Without conceding the propriety of these rejections, terminal disclaimers over each of the foregoing prior patents are filed herewith to overcome these rejections.

Rejection under 35 U.S.C. §103(a) (obviousness)

Claims 1-3 and 8-9 have been rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Eberwine (5,922,553) in view of Eberwine (7,115,371), Waggoner (5,627,027) and Sano (5,665,539). Applicants agree with the examiner that Eberwine '553

does not disclose a monoclonal antibody which binds to a selected epitope comprising a universal epitope. Eberwine '371 discloses a single chain Fv or CDR which contains a universal epitope, but it does not teach or suggest the use of biotin-streptavidin linkers to bind the Fv or CDR to the oligonucleotide. Sano discloses the use of a biotin-streptavidin linker to attach marker DNA to antibody. However, Sano does not teach or suggest the use of a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

Eberwine and Sano fail to teach the linear quantification of the molecule comprising the selected epitope by using a fluorescent stain to label the RNA amplification product. Further addition of the teaching in Waggoner does not cure the gaps in Eberwine and Sano. Examiner argues that Waggoner "discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56)." However, the passage cited in Waggoner states that "luminescent cyanine and related dyes can be attached to fragments of DNA or RNA. The labeled fragments of DNA or RNA can be used as fluorescent hybridization *probes* to identify the presence and quantity of specific complementary nucleotide sequences in samples of DNA or RNA." Therefore, Waggoner discloses the use of cyanine-*labeled RNA probes* for hybridization to a target sequence, and not the staining of *unlabeled* amplified RNA with cyanine dye. In fact, Waggoner states at column 4, lines 35-45 that "[t]his invention relates to the *covalent* reaction of highly luminescent and highly light absorbing cyanine…" (emphasis added). The use of cyanine dyes as a *stain*, as in our invention, does not involve *covalent* attachment of cyanine dyes, but rather the intercalation of the dye in the nucleic acid. (See Example 1 at page 26 in Application which refers to the use of "intercalating dye RiboGreen", which is a cyanine intercalating agent).

These facts, taken together with the other art cited by the Examiner as discussed supra, fail to support a *prima facie* case of obviousness.

Claims 4-7 have been canceled, rendering the objection to said claims moot.

Applicants respectfully submit that the present application is in condition for allowance. Favorable consideration and an early notice of allowance are respectfully requested.

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